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## ABSTRACT OF THE DISCLOSURE

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Multidomain polynucleotides responsive to signalling agents are designed and constructed to have at least three domains which can be partially or completely overlapping or nonoverlapping: an actuator (catalytic or reporter) domain, a bridging domain, and a receptor domain. In a typical embodiment, a signalling agent such as a chemical ligand interacts with the receptor domain, which changes conformation or otherwise influences the bridging domain so that the activity, catalytic, or reporter function of the actuator domain is stimulated or inhibited. In some ribozyme embodiments, for example, ligand-specific molecular sensors composed of RNA are created by coupling pre-existing catalytic and receptor domains via novel structural bridges which function such that binding of a ligand to the receptor domain triggers a conformational change within the bridge, and this structural reorganization dictates the activity of the adjoining ribozyme. Processes for allosterically selecting other multidomain polynucleotides typically involve mixing and matching domains to optimize binding or other signal response and/or reporter activity.